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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,528	BINAH ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,14,18,28,31 and 36* is/are pending in the application.

4a) Of the above claim(s) *28 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,14,18 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The Amendment filed on 11/08/2006 in response to the previous Non-Final Office Action (05/09/2006) is acknowledged and has been entered.

Claims 1, 7-9, 14, 18, 28, 31 and 36 are currently pending.

Claims 28 and 31 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 7-9, 14, 18 and 36 are currently under consideration.

(NOTE: Claim 8 is identified as currently amended, but does not appear to set forth the amendments which have been made. Upon review of Claim 8, it appears that Applicants intended to mark though "4" and insert "1", such that the claim depends from claim 1. Thus, the claims will be examined to the extent that Claim 8 recites "The anti-tumor agent of claim 1, wherein the protein is an immunoglobulin.")

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-9, 14 and 18 remain rejected and new claim 36 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. In the instant case, the claims are inclusive of a genus of anticancer agents comprising at least two proteins having a molecular weight of about 100,000 Daltons and a second protein having a molecular weight in excess of 200,000 Daltons, or a first protein having a molecular weight in excess of 150,000 Daltons and a second protein having a molecular weight in excess of 700,000 Daltons. Therefore, the claims encompass a genus of proteins defined solely by its principal biological property and approximate molecular weights, which is simply a wish to know the identity of any material with that biological property.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 2, lines 21-23) that the agents of the invention include polypeptides found in the serum of normal healthy alligators or crocodiles, characterized in that they show anti-tumor activity. For example, the specification teaches (page 16, lines 20+) that alligator serum was screened for anti-tumor activity in human tumor cell lines. Specifically, the specification teaches that based on size exclusion chromatography, it appears that the anti-tumor activity resides in a protein or proteins having a molecular weight of approximately 150,000 Daltons (page 8, lines 10-12). Specifically, the specification teaches that electrophoresis under denaturing conditions of fractions 11-12 and 13-14 which contain the anti-activity, provided two bands with anti-tumor activity, one approximately 67 kD and the second of approximately 30 kD. In addition, the specification teaches that it is clear that Serum Y, e.g., alligator serum, contains at least two factors, one factor having a molecular weight of about 150 kDa and a second having a molecular weight of about 700 kDa, that act in concert in order to exert the tumor cell killing effect (page 21, lines 15-17). Thus while the specification attempts to describe possession of a protein and/or fragments thereof in terms of function and molecular weight, there is insufficient written description encompassing a "antitumor agent derived from reptile serum comprising at least one serum protein

from normal reptile serum" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of a "anti-tumor agent" are not set forth in the specification as-filed, and therefore, is not commensurate in scope with the claimed invention. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of proteins derived from normal reptile serum that encompass the genus of anti-tumor agents nor does it provide a description of structural features that are common to the anti-tumor agents. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of anti-tumor agents, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Moreover, a lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to the rejection, Applicants assert that amended claim 1 describes the anti-tumor agent by means of the source from which it has been obtained, as well as a process by which it may be produced, so that the invention is defined by way of a product-by process format which fully enables the product. Thus, Applicants assert that the there is full enablement of the product described in the instant specification as filed.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants assertion that amended claims provide full enablement for the product, the Examiner acknowledges that Applicants have amended in a product-by-process format.

However, the Examiner recognizes that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). Thus while the specification attempts to describe possession of a protein and/or fragments thereof in terms of function and molecular weight, there is insufficient written description encompassing a "antitumor agent derived from reptile serum comprising at least one serum protein from normal reptile serum" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of a "anti-tumor agent" are not set forth in the specification as-filed, and therefore, is not commensurate in scope with the claimed invention.

New Rejections necessitated by amendment and/or upon reconsideration:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8 recites the anti-tumor agent of claim 1, wherein the protein is an immunoglobulin. However, it is unclear as to what "protein" the limitation is referring to because independent claim 1 recites two different proteins, i.e., a first protein having a molecular weight in excess of 150,000 Daltons and a second protein having a molecular weight in excess of 700,000 Daltons.

Claim 9 recites the anti-tumor agent of claim 1, wherein the protein is in essentially isolated form. However, it is unclear as to what "protein" the limitation is referring to because independent claim 1 recites two different proteins, i.e., a first protein having a molecular weight in excess of 150,000 Daltons and a second protein having a molecular weight in excess of 700,000 Daltons.

Claim 9 is further rejected because the phrase "essentially isolated form" in the second line of Claim 9 is a relative phrase which renders the claim indefinite. The phrase "essentially isolated form" is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree such that one of ordinary skill in the art would not be reasonably appraised of

the scope of the invention. In the instant case, while the specification teaches the preparation of alligator serum on page 11, lines 19-26 and further, the fractionation of alligator serum on page 13, lines 18-28, the specification does not appear to define the meets and bounds of the phrase the essentially isolated form. In other words, it is unclear what constitutes a protein in an essentially isolated form.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-9, 14 ,18 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claim 1 has been amended in a product-by-process form to recite an anti-tumor agent derived from reptile serum obtained by a process comprising the steps of: a) fractionating the serum by the addition of ammonium sulfate salt in an amount of about 45% of the amount necessary to form a saturated solution; b) centrifuging the serum to recover the precipitated proteins; c) redissolving the precipitate and desalting the recovered proteins; d) fractionating the desalted protein; and e) collecting at least one active fraction, wherein the anti-tumor agent comprises a first protein having a molecular weight in excess of 100,000 Daltons and a second protein having a molecular weight in excess of 200,000 Daltons. Applicants point to claim 26 and the specification at page 3, lines 8-9 for support for this limitation. However, the specification and claims, as originally filed, does not appear to lend support for an anti-tumor compound obtained by the claimed process wherein the anti-tumor compound comprises a first protein having a molecular weight in excess of 100,000 Daltons and a second protein having a molecular weight in excess of 200,000 Daltons. For example, the specification teaches the fractionation of alligator serum, referred to as Serum Y, using 45% ammonium sulfate precipitation to obtain a fraction referred to as Ya (page 18) which was determined to contain a protein having an approximate weight of 150 kD (page 19, lines 7-22). The

specification further teaches (page 21, lines 15-17) that it is clear that Serum Y contains at least two factors that act in concert in order to exert the tumor cell killing effect, wherein one factor has a molecular weight of about 150 kDa and the other is about 700 kDa. Thus, while the specification appears to teach that the Serum Y contains these two proteins, the specification does not appear to provide support for an anti-tumor compound obtained by the claimed process comprising comprises a first protein having a molecular weight in excess of 100,000 Daltons and a second protein having a molecular weight in excess of 200,000 Daltons. Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7-9, 14, 18 and 36 are rejected under 35 U.S.C. 102(b) as anticipated by Baril et al (Science 1961; 133: 278-279).

Baril et al. teach electrophoretic analysis of young alligator (*Alligator mississipienis*) serum. In particular, Baril et al. teach that the serum was obtained by cardiac puncture and stored (page 278, middle column, 2nd full paragraph). In addition, Baril et al. found that alligator serum has a large α-globulin to albumin ratio, wherein the alligator globulin precipitates out in 30-40 percent saturated ammonium sulfate solutions while the albumin is soluble in 50 percent saturation (page 278, 2nd column, 1st paragraph, and 3rd column, last paragraph). In the instant case, the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements. As such, the claimed limitation that the anti-tumor agent derived from reptile serum comprises a first protein having a molecular weight in excess of 1000,000 Daltons and a second protein having a molecular weight in excess of 200,000 Daltons does not appear to result in a manipulative difference between the prior art serum obtained from young alligators because the claims can reasonably encompass reptile serum

and not just the two peptides obtained therefore. In addition, although Baril et al. does not explicitly teach that the anti-tumor agent derived from serum is in essentially isolated form, the claims can reasonably be interpreted as serum removed from the body of the alligator. As such, Baril et al. meets the claimed limitation. Moreover, while Baril et al. does not explicitly teach that the alligator (*Alligator mississipienis*) serum is an anti-tumor agent or that the protein is an immunoglobulin, the claims are drawn to the product *per se* and inherently, such alligator serum would be an anti-tumor agent because the specification teaches that the alligator serum was obtained from serum derived from *Alligator mississipienis* (page 11, line 19 of specification). Thus, the claimed anti tumor agent obtained from alligator serum appears to be the same as the prior art. Moreover, while Baril et al. does not specifically teach a "pharmaceutical composition" comprising the anti-tumor agent, the claims do not appear to recite any additional ingredients, such as a pharmaceutical carrier, which are present in addition to the reptile serum protein. As such, Baril et al.. meets the claims limitation. Moreover, although Baril et al. does not specifically characterize the alligator serum as a diagnostic agent, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982) Lastly, even though the product-by-process claim of Claim 1 is limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

Therefore, No claim is allowed.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
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Art Unit 1642

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